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Proposed Re-evaluation Decision

Hexazinone

(publié aussi en français)

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide hexazinone, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing hexazinone in Canada.

An evaluation of available scientific information found that products containing hexazinone do not present unacceptable risks to human health or the environment when used according to label instructions. As a condition of the continued registration of hexazinone uses, new risk-reduction measures must be included on the labels of all products. Additional data are being requested as a result of this re-evaluation.

This proposal affects all end-use products containing hexazinone registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document¹ that summarizes the science evaluation for hexazinone and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of hexazinone.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive *DIR2001-03, PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Hexazinone is one of the active ingredients to be re-evaluated during the current re-evaluation cycle.

¹ "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Hexazinone has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMPP]).

On the basis of health and environmental risk assessments published in the 1994 RED and the 2002 Tolerance Reassessment Eligibility Document (TRED) for hexazinone, the USEPA concluded that hexazinone was eligible for reregistration with implementation of risk-reduction measures. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in the RED and TRED documents were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What is Hexazinone?

Hexazinone is a non-selective herbicide that is used to control broadleaf weeds and woody plant species in cropland and non-cropland areas, and as a selective herbicide in woodland management practices. It is registered for use on alfalfa, blueberries, Christmas tree plantations, woodland management areas and in non-cropland areas such as railroad, highways, utility and pipeline rights-of-way, petroleum tank farms, storage areas, industrial plant sites and other similar areas. Hexazinone is applied by ground or aerial equipment. Aerial applications are solely for site preparation in woodland management areas. Applications are made by farm workers and professional applicators.

Health Considerations

Can Approved Uses of Hexazinone Affect Human Health?

Hexazinone is unlikely to affect your health when used according to the revised label directions.

People could be exposed to hexazinone by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that hexazinone was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions were considered to be applicable to the Canadian situation, and equivalent risk reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Hexazinone is currently registered in Canada for use on alfalfa and blueberries and could be used in other countries on crops that are imported into Canada. There are no specific Canadian MRLs established for hexazinone. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in the Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

Environmental Considerations

What Happens When Hexazinone Is Introduced Into the Environment?

Hexazinone is unlikely to affect non-target organisms when used according to the revised label directions.

Non-target organisms such as birds, mammals, insects, aquatic organisms and terrestrial plants could be exposed to hexazinone in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. The resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a low risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistration of hexazinone was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required. Furthermore, the PMRA will require aquatic and terrestrial buffer zones for end-use products containing hexazinone used as liquids to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of hexazinone, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional protective equipment to protect mixer/loader/applicators
- A restricted-entry interval to protect workers re-entering treated sites

Environment

- Additional advisory label statements to reduce potential surface and groundwater contamination
- Buffer zones to protect non-target, sensitive aquatic and terrestrial habitats

What Additional Scientific Information is Being Requested?

Data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter.

Based on the USEPA review of their environmental fate data, hexazinone could leach into groundwater and can runoff or drift into surface water. Data to confirm that acceptable levels of hexazinone and its metabolites in groundwater and surface water are not exceeded are required. These include any existing Canadian water monitoring data. A scientific rationale to show the relevance of existing American monitoring data to Canada may be acceptable. This rationale should include information on hexazinone use in Canada (e.g. areas of use, quantity used, typical application rates), and establish the vulnerability of areas of use to groundwater contamination (i.e. provide information on soil type and groundwater depth in areas of use).

Appendix IV lists all data requirements.

Next Steps

Before making a final re-evaluation decision on hexazinone, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision² document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

²

"Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

Hexazinone is a herbicide that acts by inhibiting photosynthesis in target plants. It is activated by rainfall or irrigation water.

Following the re-evaluation announcement for hexazinone, the registrant of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the labels of commercial and end-use products.

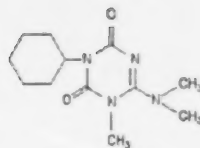
The PMRA used recent assessments of hexazinone from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for hexazinone, dated 1994, and the USEPA Tolerance Reassessment Eligibility Document (TRED) (USEPA 2002) as well as other information on the regulatory status of hexazinone in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Hexazinone
Function	Herbicide
Chemical family	Triazine
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	3-cyclohexyl-6-dimethylamino-1-methyl-1,3,5-triazine-2,4(1 <i>H</i> ,3 <i>H</i>)-dione
2 Chemical Abstracts Service (CAS)	3-cyclohexyl-6-(dimethylamino)-1-methyl-s-triazine-2,4(1 <i>H</i> ,3 <i>H</i>)-dione
CAS Registry Number	18019315
Molecular formula	C ₁₂ H ₂₀ N ₄ O ₂

Structural formula



Molecular weight	252.3
Purity of the technical grade active ingredient	98.7% nominal (lower limit: 95.75%; upper limit: 100%)
Registration Number	19544

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	1×10^{-6} – 3.9×10^{-5} mmHg
Solubility in water	33 g/L at 25°C
<i>n</i> -octanol–water partition coefficient	$\log K_{ow} = 1.18$

2.3 Comparison of Use Patterns in Canada and the United States

Hexazinone is a herbicide registered in Canada for general weed control. It is used as a non-selective herbicide in cropland and non-cropland areas, and as a selective herbicide in woodland management practices. It acts by inhibiting photosynthesis in the target plants. Rainfall or irrigation water is needed to activate it. It is used on alfalfa, blueberries, Christmas tree plantations, woodland management areas and in non-cropland areas (railroad, highway, utility and pipeline rights-of-way, petroleum tank farms, storage areas, industrial plant sites and other similar sites). It is applied during active plant growth, early in the season (spring), and provides pre-emergent or postemergent control of undesirable vegetation. Hexazinone is applied once per year with an application rate of up to 2.03 kg a.i./ha for food/feed crops, up to 4.32 kg a.i./ha for

reforestation programs and up to 8.1 kg a.i./ha for non-cropland areas. The end-use products are formulated as liquids, wettable powders and soluble granules and are applied using fixed boom, hand-spray, sprinkling can or aerial equipment. Aerial applications are solely for site preparation in woodland management areas.

The American and Canadian use patterns were compared. The formulation types of end-use products and use sites in Canada are among those registered in the United States. Other uses of hexazinone registered in the United States, but not in Canada are, on pineapple and sugarcane, rangeland and pastures, ornamental plants and as a harvesting aid in harvesting wood pulp used in the manufacture of paper.

The rates assessed in the RED (i.e. 1.7 kg a.i./ha for food/feed uses and up to 13.5 kg a.i./ha for non-cropland) encompass the maximum Canadian application rates (i.e. 2.03 kg a.i./ha for food/feed crops, 4.32 kg a.i./ha for reforestation programs and 8.1 kg a.i./ha for non-cropland areas). The number of applications permitted in the United States (one application per year) encompasses the number of applications in Canada. The Canadian application methods are among those registered in the United States. Based on this comparison of use patterns, it was concluded that the USEPA RED for hexazinone is an adequate basis for the re-evaluation of uses of hexazinone in Canada.

All current uses are being supported by the registrant and were therefore considered in the re-evaluation of hexazinone. Appendix II lists all hexazinone products that are registered under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 1994 RED, the USEPA concluded that the end-use products formulated with hexazinone registered at the time would not pose unreasonable risks or adverse effects to humans and the environment and were eligible for reregistration. After the RED, the USEPA published a TRED in 2002 that includes an aggregate risk assessment that met the *Food Quality Protection Act* requirements.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to hexazinone may occur through consumption of food and water, through residential exposure, while working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required. The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix III.

Workers can be exposed to hexazinone when mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

It was determined that, in addressing potential exposure scenarios for occupational handlers of hexazinone, concerns were predominantly related to skin contact. As hexazinone is poorly absorbed through the skin, little or no absorption is anticipated. It was also determined that there were no relevant endpoints of toxicological concern and therefore a quantitative exposure and risk assessment was not conducted.

3.1.1.2 Postapplication Exposure and Risk

The USEPA did not assess occupational postapplication risks to agricultural workers because no dermal endpoint of concern was identified. In lieu of a postapplication risk assessment a restricted-entry interval of 48 hours for all hexazinone use products was required. This included end-use products used for:

- commercial and research uses on farms, forests, nurseries and greenhouses to produce agricultural plants, including food, feed, and fibre plants, trees, turf grass, flowers, shrubs, ornamentals and seedlings; and
- soil or planting medium in which the plants are or will grown.

This was based on the Worker Protection Standard as hexazinone is in Toxicity Category I for primary eye irritation.

This was considered applicable to the Canadian situation, and the PMRA requires a 48 hour restricted-entry interval to further protect workers from postapplication exposure. Proposed label amendments are listed in Appendix IV.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

There are no residential uses registered in Canada, and hexazinone is not intended for use in residential areas.

3.1.2.2 Exposure from Food and Drinking Water

Acute dietary risk is calculated considering the highest ingestion of hexazinone that would be likely on any one day and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of hexazinone residue that might be consumed in a day. A value representing the high end (99.9th percentile) of this distribution is compared to the acute reference dose, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the acute reference dose, acute dietary exposure is considered acceptable.

No effects attributed to a single exposure were identified for the general population; however, the toxic endpoint for acute dietary exposure concerned in utero exposure. Therefore, the acute dietary exposure and risk assessment included only females 13–50 years. The acute toxicological endpoint of concern was based on a rat development study. The calculated acute dietary risk estimate was <1.0 % of the acute population adjusted dose for the population subgroup consisting of females aged 13–50 years.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it was expressed as the chronic population adjusted dose. The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix III).

The toxicological endpoint of concern for chronic toxicity was based on a one-year feeding study in dogs (liver effects in males and females). Exposures, as percentages of the chronic population adjusted dose, ranged from 3% for females aged 13–50 years to 15% for children aged 1–6 years.

The USEPA used a Tier I modelling system (FIRST) to estimate the environmental concentrations for hexazinone (including its degradates) in surface waters. FIRST assumed 100% crop treatment, aerial application to alfalfa (the food/feed item with the greatest percent of crop treated with hexazinone) at a rate of 1.7 kg a.i./ha, applied once per year, and no soil incorporation after application. The FIRST peak water-surface water concentration for the acute scenario was 129.8 ppb and for the chronic scenario, 47.1 ppb; modelling estimated environmental concentrations (EECs) were higher than monitoring EECs, and were considered a conservative estimation. The EECs from groundwater were estimated using an available

small-scale prospective groundwater monitoring study in California where hexazinone was broadcast at a rate of 0.84 kg a.i./ha on an alfalfa crop in an area of sandy soil. The application was not soil-incorporated. The groundwater residue concentration for hexazinone, based on the groundwater prospective monitoring study, was 41.8 ppb. Monitoring data was also available from Maine, but these were used for comparison purposes only. Drinking water levels of comparison (DWLOC) were calculated. The USEPA concluded that for acute drinking water risk, potential peak EECs in surface water (modelling) and EECs in groundwater (monitoring data) were below the acute DWLOC for females (13–50 years). For chronic drinking water risk, the average EECs of hexazinone in groundwater or surface water were below the chronic DWLOC for all population subgroups and therefore below the USEPA's level of concern.

The USEPA assessment encompasses the current registered uses of hexazinone in Canada. The American assessment is considered relevant to Canada because it was a conservative, Tier I, dietary risk assessment using tolerance levels and the assumption that 100% of the crop was treated. Furthermore, risk was estimated to be less than 1% of the acute population adjusted dose for the most sensitive population subgroup and from 3–15% of the chronic population adjusted dose. The American tolerances used in the risk assessment were equal to Canadian MRLs (i.e. 0.1 ppm general MRL³). The modelled estimated drinking water concentration was based on worst case scenarios encompassing Canadian application rates. Therefore, the USEPA assessment is considered applicable for the Canadian situation.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to hexazinone (i.e. from food, water and residential exposures).

Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures.

Short-term and intermediate aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

The American aggregate risk assessment included dietary risk due to food and drinking water. It is considered to be relevant to Canada for the following reasons.

- The American use pattern assessed in the RED encompasses the use pattern currently registered in Canada.
- A conservative, 1st Tier, unrefined estimate of dietary exposure from food (assuming tolerance residues and 100% crop treatment) was used and there were no concerns regarding dietary risk for all population subgroups.

³ Changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of hexazinone in Canada.

3.1.3 Cumulative Effects

The USEPA has not determined whether hexazinone has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that hexazinone does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

The RED indicated that hexazinone exhibits properties of a substance found in groundwater and, indeed, had been detected in groundwater; hence, the USEPA recommended that all product labels carry a groundwater advisory. Canadian labels for end-use products containing hexazinone must also include a groundwater advisory.

On the east coast of Canada, hexazinone is applied to blueberries which grow on coarse, shallow soils⁴. As the environmental fate data shows that the herbicide hexazinone is leachable, this is considered a factor of concern. Hexazinone has been detected in groundwater in Canada (New Brunswick, Nova Scotia, Prince Edward Island) as well as Maine and in several other states in the United States (according to the USEPA RED). No Canadian water quality guideline exists for hexazinone.

Presently a groundwater quality monitoring study is being undertaken in New Brunswick². The study has been designed to:

- provide data on pesticides leaching from non-point sources;
- document hydrogeological conditions prevailing at and in the vicinity of the sampling well; and
- confirm or give further insight into the likely cause of contamination.

3.2.1 Environmental Risk Assessment

The USEPA concluded that hexazinone is stable to hydrolysis (pH levels 5, 7, and 9) under normal environmental conditions and stable to aqueous photolysis (pH 7). When applied to sandy loam soil, hexazinone had a reported half-life of 228 days. Degradation in aerobic soil was mainly as a result of microbiological activity, and half-lives were reported to be 216 and

⁴ Agriculture and Agri-Food Canada, www.agr.gc.ca, Pesticides.

1440 days in non-sterile and sterile sandy loam soils, respectively. Hexazinone had reported half-lives of 230 days and >1500 days when applied to non-sterile and sterile sediment pond water, respectively, and exposed to anaerobic conditions. Aerobic aquatic metabolism resulted in a half-life of >2 months.

In leaching/adsorption/desorption studies, it was found that hexazinone weakly adsorbed to sandy loam and silt loam soil, and strongly adsorbed to loam soil. Furthermore, it was found that hexazinone and its major soil degradates ranged from immobile to mobile. Field dissipation studies in Newark, Delaware, and Greenville, Mississippi, indicated that hexazinone did not move below the top 30 cm of the soil; however, metabolites leached to a depth of 75 cm in soil. A forestry dissipation study indicated that hexazinone moved off-site through leaching and runoff and that hexazinone was observed in soil at depths of >30 cm. In addition, hexazinone was detected in runoff water up to 6 months postapplication.

Based on laboratory data and confirmed by field and forestry data, hexazinone appeared to be persistent and mobile in soil and aquatic environments. The degradates also appeared to be persistent and mobile.

The USEPA concluded that hexazinone may contaminate surface water by spray drift at application and post-application via runoff. In addition, hexazinone may be persistent in some receiving surface waters low in microbiological activities or areas that have long hydrological resident times. The USEPA found that hexazinone was reported in runoff water up to 6 months after treatment in a forestry dissipation study.

Hexazinone was evaluated for persistence and mobility in relation to its potential to contaminate groundwater. The USEPA concluded that hexazinone exhibited many of the properties and characteristics associated with chemicals that have been detected in groundwater. It was found that there was a strong possibility that hexazinone could move to groundwater, especially in vulnerable areas. Groundwater contamination has been reported in Hawaii, Florida, Maine and North Carolina. Based on this information, groundwater monitoring information was requested to determine the potential of this chemical to leach to groundwater and a groundwater advisory was required on all hexazinone end-use products.

To assess the ecological risk of hexazinone to terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern.

Hexazinone is registered for numerous outdoor uses in the United States, including agricultural crops such as alfalfa and blueberries. Exposure to non-target organisms was expected to be acute and chronic and would result from direct applications, spray drift and runoff from treated areas.

In the quantitative risk assessment, exposure estimates, used to calculate RQs, were based on expected runoff from ground and aerial applications as well as drift from aerial applications.

Results for application of granular formulations (maximum application rate of 13.5 kg a.i./ha) indicated the following:

- The endangered species level of concern (LOC) for birds was exceeded at use rates of ≥ 4.5 kg a.i./ha and the restricted use LOC was exceeded at use rates of ≥ 8.0 kg a.i./ha. No chronic effects for birds were expected even when application rates exceeded 7.0 kg a.i./ha as application was once per year, and hexazinone displayed low bioaccumulation.
- The endangered species LOC was exceeded for small mammals at use rates of ≥ 4.0 kg a.i./ha; the restricted use LOC was exceeded at use rates of ≥ 7.0 kg a.i./ha and the high risk LOC was exceeded at use rates of ≥ 13.5 kg a.i./ha.
- No acute LOCs for fish or aquatic invertebrates were exceeded with an application rate of 15.0 kg a.i./ha for ground use and an application rate of 1.7 kg a.i./ha for aerial use. Chronic LOCs for fish or aquatic invertebrates were not exceeded.
- LOCs for endangered and non-endangered aquatic and terrestrial plants were exceeded at all application rates for both ground and aerial applications.

To address the risk to non-target plants and small animals the USEPA recommended a rate reduction (not applicable to Canada).

The American use pattern for hexazinone encompasses the Canadian use pattern, and the USEPA's risk-reduction measures should be applied to Canadian hexazinone products. The USEPA mitigation measures must be adapted to the Canadian situation as follows.

- A groundwater advisory statement is required on all Canadian end-use labels.
- A statement regarding runoff is required on all Canadian end-use labels.
- The PMRA is requiring the statement "Toxic to non-target terrestrial and aquatic plants." on the label of all end-use products to protect the environment, .
- The PMRA will require terrestrial and aquatic buffer zones for the formulations of hexazinone used as liquids to protect aquatic organisms and terrestrial plants from spray drift. Proposed label amendments are listed in Appendix IV. Inputs to buffer zone models are presented in Appendix V.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of hexazinone. The PMRA has reached the following conclusions.

- Hexazinone is not bioaccumulative; the *n*-octanol–water partition coefficient ($\log K_{ow}$) is 1.18, which is below the TSMP Track 1 cut-off criterion of ≥ 5.0 . Hexazinone does not meet all Track 1 criteria; thus, it is not a candidate for Track 1 classification.
- Based on a review of the available chemistry information (see Section 2.1), the technical grade active ingredient is not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II.
- The technical grade active ingredient is not expected to contain other impurities of human health or environmental concern as identified in DIR98-04, Section 2.13.4, or TSMP Track 1 substances as identified in DIR99-03, Appendix II.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*, published on 31 May 2006.

4.0 Proposed Re-evaluation Decision

The PMRA has determined that hexazinone is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products must be amended to include label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical active ingredient is required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

5.0 Data Required as a Condition of Continued Registration

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient must provide these data within the timeline specified in the decision letter that the PMRA will send to registrants of the technical grade active ingredient.

- Based on the USEPA review of their environmental fate data, hexazinone has the potential to leach into groundwater and can runoff or drift into surface water. Data to confirm that acceptable levels of hexazinone and its metabolites in groundwater and surface water are not exceeded are required. A scientific rationale to show the relevance of existing American monitoring data to Canada may be acceptable. This rationale should include information on hexazinone use in Canada (e.g. areas of use, quantity used, typical application rates) and establish the vulnerability of areas of use to groundwater contamination (i.e. provide information on soil type and groundwater depth in areas of use). Any existing Canadian water monitoring data is also required (including the groundwater quality monitoring study being undertaken in New Brunswick).
- DACO 9.8.4: Terrestrial Vascular Plants - Seedling Emergence (USEPA OPPTS 850.4100 guideline) and Vegetative Vigour (USEPA OPPTS 850.4150 guideline)].

6.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED and TRED documents for hexazinone is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
aPAD	acute population adjusted dose
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
cPAD	chronic population adjusted dose
DACO	data code
DWLOC	drinking water level of comparison
EEC	expected environmental concentration
EXAMS	Exposure Analysis Modeling System
FIRST	FQPA Index Reservoir Screening Tool
FQPA	<i>Food Quality Protection Act</i>
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	<i>n</i> -octanol–water partition coefficient
L	litre(s)
LEACHM	Leaching Estimation and Chemistry Model
LC ₅₀	lethal concentration to 50%
LOC	level of concern
mg	milligram(s)
mm	millimetre(s)
MOE	margin of exposure
MRL	maximum residue limit
NOEL	no observed effect level
OPPTS	Office of Prevention, Pesticides and Toxic Substances
PDI	potential daily intake
pH	-log ₁₀ hydrogen ion concentration
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
ppm	parts per million
Q ₁ *	cancer potency factor
RED	Reregistration Eligibility Decision
RfD	reference dose
RQ	risk quotient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of this active ingredient are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter.

- Data to confirm that acceptable levels of hexazinone and its metabolites in groundwater and surface water are not exceeded;
- Any existing Canadian water monitoring data (including the groundwater quality monitoring study being undertaken in New Brunswick);
- DACO 9.8.4: Terrestrial Vascular Plants - Seedling Emergence (USEPA OPPTS 850.4100 guideline) and Vegetative Vigour (USEPA OPPTS 850.4150 guideline)].

These studies must be conducted according to the appropriate OPPTS guidelines indicated.

Should the registrant fail to submit these studies within the specified timeline, conservative buffer zones for the protection of sensitive aquatic habitats will be required on product labels.

Appendix II Registered Hexazinone as of 25 June 2007

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
14163	Commercial	E.I. Du Pont Canada Company	Velpar Herbicide Weed Killer	Soluble powder	90
18197	Commercial Restricted	E.I. Du Pont Canada Company	Velpar L Herbicide (Water Dispersable Solution)	Liquid	25
19544	Technical	E.I. Du Pont Canada Company	Hexazinone Technical Herbicide	Solid	98.7
21390	Commercial Restricted	E.I. Du Pont Canada Company	Dupont Pronone 10G Granular Herbicide	Granular	10
21534*	Commercial	E.I. Du Pont Canada Company	Velpar 90 Herbicide in Toss-n-Go Bags	Soluble powder	90
24587*	Commercial	E.I. Du Pont Canada Company	Velpar ULW Herbicide	Soluble granules	75
25225	Commercial Restricted	E.I. Du Pont Canada Company	Velpar DF Herbicide Water Dispersible Granule	Wettable granules	75
27551	Manufacturing concentrate	E.I. Du Pont Canada Company	Hexazinone 90SP MUP	Soluble powder	90

* Discontinued products.

Appendix III Toxicological Endpoints for Hexazinone Health Risk Assessments

Exposure Scenario (route and period of exposure)	Dose (mg/kg bw/day)	Study	Target UF/SF or MOE or Q ₁ ^a
Acute Oral	NOEL = 400	Developmental toxicity study in rat	100
	RfD = 4.0 aPAD = 4.0		
Chronic Oral	NOEL = 5	1-year feeding study in dog	100
	RfD = 0.05 cPAD = 0.05		

^a UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments; Q₁* refers to cancer potency factor.

Appendix IV Label Amendments for Products Containing Hexazinone

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following statement must be included in a section entitled **PRECAUTIONS**.

Wear a long-sleeved shirt, long pants and shoes plus socks during application. In addition, wear chemical-resistant gloves and goggles or a face shield during mixing/loading, clean-up or repair activities and when using handheld application equipment.

- For **granular** end-use products used on alfalfa, blueberries, Christmas tree plantations, conifer release, forest plantings [reforestation programs], the following statement must be included.

Do not enter or allow entry into treated area until 48 hours after application.

- For end-use products used as **liquids** on non-cropland areas (railroad, highway, utility and pipeline rights-of-way, petroleum tank farms, storage areas, industrial plant sites and other similar sites), following statement must be included.

Do not enter or allow worker entry into treated areas until 12 hours after application or until sprays have dried.

II) The following statements must be included in the section entitled **DIRECTIONS FOR USE**.

- The following buffer zone statements must appear on all formulations (except granulars).

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural and Biological Engineers (ASABE) medium classification.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural and Biological Engineers (ASABE) medium classification. **DO NOT** allow nozzle spacing to exceed 65% of boom length.

Buffer Zones

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, rangelands, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs, and wetlands), and estuarine/marine habitats.

For application to rights-of-way, buffer zones for protection of sensitive terrestrial habitats are not required; however, the best available application strategies which minimize off-site drift, including meteorological conditions (e.g. wind direction, low wind speed) and spray equipment (e.g. coarse droplet sizes, minimizing height above canopy), should be used. Applicators must, however, observe the specified buffer zones for protection of sensitive aquatic habitats.

Method of application	Use Site		Buffer Zones (metres) Required for the Protection of:					
			Freshwater Habitat of Depths:			Estuarine/Marine Habitats of Depths:		
			Less than 1 m	1-3 m	Greater than 3 m	Less than 1 m	1-3 m	Greater than 3 m
Field sprayer*	Woodland Management, Reforestation		5	1	0	3	1	0
	Christmas Tree Plantations, Conifer Release		3	1	0	2	1	0
	Alfalfa		1	0	0	1	0	0
	Blueberries		2	1	0	2	1	0
	Non-crop areas		5	2	1	5	2	1
Aerial	Woodland Management, Reforestation (Reg. No. 18197)	Fixed wing	750	225	70	525	225	70
		Rotary wing	475	125	45	325	125	45
	Woodland Management, Reforestation (Reg. No. 25225)	Fixed and Rotary wing	600	125	45	375	125	45

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy or ground, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy or ground, the labelled buffer zone can be reduced by 30%.

** Terrestrial buffer zones are not required for rights-of-way.

III) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

Hexazinone demonstrates the properties and characteristics associated with chemicals detected in groundwater. The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the water table is shallow.

To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted, fine textured, or low in organic matter such as clay).

Avoid application of this product when heavy rain is forecast.

Toxic to non-target terrestrial and aquatic plants.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements, and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Appendix V Inputs to Buffer Zone Models

Ground Use Data (from Canadian labels)				
Crop	Formulation Type	Method of Application	Number of Application	Maximum Application Rate (g a.i./ha)
Woodland management, Reforestation	End-use product used as liquid	Field sprayer (ASABE medium)	1	4320
Christmas trees, Conifer release	End-use product used as liquid	Field sprayer (ASABE medium)	1	1992
Alfalfa	End-use product used as liquid	Field sprayer (ASABE medium)	1	1010
Blueberries	End-use product used as liquid	Field sprayer (ASABE medium)	1	2030
Non-cropland	End-use product used as liquid	Field sprayer (ASABE medium)	1	8010

Model Input Data for Aquatic Buffer Zones (from 2005 RED)		
Half-life for aquatic buffer zones	60 days	
Most sensitive freshwater species	<i>Anabaena flos-aquae</i>	1/10 LC ₅₀ = 0.21 mg a.i./L
Most sensitive estuarine/marine species	<i>Anabaena flos-aquae</i>	1/10 LC ₅₀ = 0.21 mg a.i./L

Model Input Data for Terrestrial Buffer Zones (from 2005 RED)		
Half-life for terrestrial buffer zones	Soil degradation half-life	216 days
Most sensitive terrestrial plant species EC ₂₅ for vegetative vigour	Tomato - seedling emergence	7.2 g a.i./ha

Aerial Use Data (from Canadian Labels)				
Crop	Formulation Type	Registration No.	Number of Applications	Rate of Application (g a.i./ha)
Woodland management, conifer release	Water dispersible granule	18197	1	4320
Woodland management, conifer release	Water dispersible solution	25225	1	4320

Product Information for Aerial Use	
Parameter	Value
Registration No. 18197	
Aircraft type	Fixed and/or rotary
ASABE spray quality	Medium
Carrier	Water
Product guarantee (g a.i./L)	240
Specific gravity of end-use product (g/L)	970
Minimum spray volume (L/ha)	35
Water content of product (%)	0
Wind speed (km/h)	16
Temperature (°C)	25
Relative humidity (%)	50
Registration No. 25225	
Aircraft type	Fixed and/or rotary
ASABE spray quality	Medium
Carrier	Water
Product guarantee (g a.i./L)	750
Specific gravity of end-use product (g/L)	1000
Minimum spray volume (L/ha)	35
Water content of product (%)	0
Wind speed (km/h)	16
Temperature (°C)	25
Relative humidity (%)	50